

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
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## PCT

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference <b>PCT 21456Y</b>		Date of mailing (day/month/year) <b>04 MAR 2005</b> <b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. <b>PCT/US04/20525</b>	International filing date (day/month/year) <b>25 June 2004 (25.06.2004)</b>	Priority date (day/month/year) <b>01 July 2003 (01.07.2003)</b>
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): A61K 31,18, 31/234, 31/24, 31/40, 31/445; C07C 63/00, 303/00; C07D 207/18, 211/06 and US Cl.: 514/330, 423, 532, 540, 602, 603; 546/226; 548/565; 562/405, 433, 450; 564/84</b>		
Applicant <b>MERCK &amp; CO</b>		

**1. This opinion contains indications relating to the following items:**

- |                                     |              |                                                                                                                                                                      |
|-------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion                                                                                                                                                 |
| <input type="checkbox"/>            | Box No. II   | Priority                                                                                                                                                             |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                     |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention                                                                                                                                           |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited                                                                                                                                              |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application                                                                                                                     |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application                                                                                                                |


**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <div style="text-align: center;">   <b>Cella Chang</b> </div> Telephone No. 703-308-1235
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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/20525

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims <u>1-14</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-14</u>	NO
Industrial applicability (IA)	Claims <u>1-14</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-14 meet the criteria set out in PCT Article 33(2), because the prior art does not teach or fairly suggest the claims.

Claims 1-14 lack an inventive step under PCT Article 33(3) as being obvious over Varghese et al CA 139:230480 in view of Rubini et al.. The instant claims are drawn to the isosteric methylene oxy compounds of Varghese et al. The isosteric methylene oxy analogs of the known compounds are expected to have similar biological activities.

Claims 1-14 meet the criteria set out in PCT Article 33(4), and thus can be used for industrial applicability because the subject matter claimed can be made or used in industry.